

IN THE CLAIMS:

This claim listing replaces all prior versions and listings of claims.

1. (Original) A gene examining apparatus utilizing a computer, the apparatus comprising:

(1) DNA microarrays in each of which a large number of fine liquid accommodating sections are two-dimensionally arranged so that openings of the fine liquid accommodating sections are located on the same plane, in which each of the liquid accommodating sections can three-dimensionally accommodate a liquid, and in which hybridization reaction occurs in the liquid accommodating section between a target nucleic acid already labeled with an optical marker substance and the nucleic acid probe; and

(2) a microscope comprising a stage supporting the DNA microarrays set forth in (1), a temperature regulating section that regulates the temperature of each DNA microarray, and imaging means for picking up an image of an optical signal from the DNA microarray.

2. (Original) The gene examining apparatus utilizing a computer according to claim 1, wherein the DNA microarray comprises a porous film having a branching channel, and the nucleic acid probe is immobilized on an inner wall of the channel in the porous film.

3. (Original) The gene examining apparatus utilizing a computer according to claim 1, further comprising:

(a) an input section which is used by an operator to input information to a computer integrally controlling the gene examining apparatus; and

(b) a display section which displays an image picked up by the imaging means.

4. (Original) The gene examining apparatus utilizing a computer according to claim 1, further comprising an image processing section which determines the intensity of an optical signal for each of the probe spots on the basis of the image picked up by the imaging means.

5. (Original) A method of examining a gene using the apparatus according to claim 1, the method comprising;

- (1) amplifying a nucleic acid extracted from a tissue or a cell obtained from a subject and adding an optical marker substance as a marker substance to afford a labeled nucleic acid;
- (2) adding the labeled nucleic acid obtained in (1) to a DNA microarray comprising a desired nucleic acid probe;
- (3) using the DNA microarray in (2) to cause hybridization reaction under desired conditions;
- (4) measuring the intensity of an optical signal from the optical marker substance in the DNA microarray obtained in (3); and
- (5) on the basis of the intensity of the optical signal obtained in (4), determining the amount of an expressed gene and/or whether or not any mutated gene is present, to obtain results of gene examinations.

6. (Original) A method of examining a gene using the apparatus according to claim 1, the method comprising;

- (1) amplifying a nucleic acid extracted from a tissue or a cell obtained from a subject and adding an optical marker substance as a marker substance to afford a labeled nucleic acid;
- (2) adding the labeled nucleic acid obtained in (1) to a DNA microarray comprising a desired nucleic acid probe;
- (3) using the DNA microarray in (2) to cause hybridization reaction under desired conditions;
- (4) after the reaction in (3) has been finished, collecting a solution contained in the DNA microarray, at the bottom of the array;
- (5) measuring the intensity of an optical signal from the optical marker substance in the DNA microarray obtained in (3);
- (6) agitating again the liquid collected at the bottom of the array in (4);
- (7) using the DNA microarray in (6) to repeat hybridization reaction under desired conditions as required;
- (8) measuring the intensity of an optical signal from the DNA microarray obtained in (6); and

(9) on the basis of the intensities of the optical signals obtained in (4) and (8), determining the amount of an expressed gene and/or whether or not any mutated gene is present, to obtain results of gene examinations.

7. (Original) The method according to claim 5, further comprising comparing information obtained by determining, on the basis of the intensity of the optical signal obtained in (4), the amount of an expressed gene and/or whether or not any mutated gene is present, with well-known information disclosed in a database and/or information obtained from a standard sample, thereby obtaining the results of gene examinations.

8. (Original) The method according to claim 6, wherein operations from (5) to (8) are repeated twice or more.

9. (Currently amended) A gene examining apparatus ~~utilizing a computer, the apparatus comprising:~~

~~(1) DNA microarrays in each of which a large number of fine liquid accommodating sections are two dimensionally arranged so that openings of the fine liquid accommodating sections are located on the same plane, in which each of the liquid accommodating sections can three dimensionally accommodate a liquid, and in which hybridization reaction occurs in the liquid accommodating section between a target nucleic acid already labeled with an optical marker substance and the nucleic acid probe;~~

~~—— (2) a microscope comprising a stage supporting the DNA microarrays set forth in (1), a temperature regulating section that regulates the temperature of each DNA microarray, and imaging means for picking up an image of an optical signal from the DNA microarray; and~~

~~—— (3) fluid transporting section connected to the DNA microarray arranged on the stage of the microscope set forth in (2), to move a fluid into and out of the DNA microarray.~~

a DNA microarray including:

a plurality of liquid accommodating sections, and

a porous film to contact with said liquid in the liquid accommodating section,

wherein openings of said liquid accommodating sections are located on the same plane and said porous film has channels provided with the fluid;

a microscope to observe the plane where said openings are located;
a fluid transporting section that moves the fluid into and out of said DNA microarray; and
a computer that controls picking up an image with said microscope and moving the fluid
with said fluid transporting section.

10. (Currently amended) The gene examining apparatus utilizing a computer according to claim 9, wherein the DNA microarray comprises a porous film having a branching channel, and the nucleic acid probe is immobilized on an inner wall of the channel in the porous film each of said channels.

11. (Currently amended) The gene examining apparatus utilizing a computer according to claim 9, wherein said microscope has an imaging means for picking up an image of an optical signal from the DNA microarray, and the gene examining apparatus further comprises a display section which displays an image picked up by said imaging means.—further comprising:
——(a) an input section which is used by an operator to input information to a computer integrally controlling the gene examining apparatus; and
——(b) a display section which displays an image picked up by the imaging means.

12. (Currently amended) The gene examining apparatus utilizing a computer according to claim [[9]]11, further comprising an image processing section which determines the intensity of anthe optical signal for each of the probe spots on the basis of the image picked up by the imaging means.

13. (Currently amended) A method of examining a gene using the apparatus according to claim 9, the method comprising;
(1) amplifying a nucleic acid extracted from a tissue or a cell obtained from a subject and adding an optical marker substance as a marker substance to afford a labeled nucleic acid;
——(2) adding the labeled nucleic acid obtained in (1) to a DNA microarray comprising a desired nucleic acid probe;
——(3) using the DNA microarray in (2) to cause hybridization reaction under desired conditions;

~~—— (4) measuring the intensity of an optical signal from the optical marker substance in the DNA microarray obtained in (3); and~~

~~—— (5) on the basis of the intensity of the optical signal obtained in (4), determining the amount of an expressed gene and/or whether or not any mutated gene is present, to obtain results of gene examinations.~~

a step of providing said DNA microarray with a fluid which includes a nucleic acid added with an optical marker substance; and

a step of picking up the image of the DNA microarray with said microscope.

14. (Currently amended) ~~A~~The method of examining a gene using the apparatus according to claim [[9]]13, further comprising a step of withdrawing the fluid from the DNA microarray through said fluid transporting section after the step of providing, but before the step of picking up the image is performed.~~the method comprising;~~

~~—— (1) amplifying a nucleic acid extracted from a tissue or a cell obtained from a subject and adding an optical marker substance as a marker substance to afford a labeled nucleic acid;~~

~~—— (2) adding the labeled nucleic acid obtained in (1) to a DNA microarray comprising a desired nucleic acid probe;~~

~~—— (3) using the DNA microarray in (2) to cause hybridization reaction under desired conditions;~~

~~—— (4) after the reaction in (3) has been finished, collecting a solution contained in the DNA microarray, at the bottom of the array;~~

~~—— (5) measuring the intensity of an optical signal from the optical marker substance in the DNA microarray obtained in (3);~~

~~—— (6) agitating again the liquid collected at the bottom of the array in (4);~~

~~—— (7) using the DNA microarray in (6) to repeat hybridization reaction under desired conditions as required;~~

~~—— (8) measuring the intensity of an optical signal from the DNA microarray obtained in (3); and~~

~~—— (9) on the basis of the intensities of the optical signals obtained in (4) and (8), determining the amount of an expressed gene and/or whether or not any mutated gene is present, to obtain results of gene examinations.~~

15-16. (Cancelled)

17. (Original) A gene examining apparatus utilizing a computer, the apparatus comprising:

(1) DNA microarrays in each of which a large number of fine liquid accommodating sections are two-dimensionally arranged so that openings of the fine liquid accommodating sections are located on the same plane, in which each of the liquid accommodating sections can three-dimensionally accommodate a liquid, and in which hybridization reaction occurs in the liquid accommodating section between a target nucleic acid already labeled with an optical marker substance and the nucleic acid probe;

(2) a microscope comprising a stage supporting the DNA microarrays set forth in (1), a temperature regulating section that regulates the temperature of each DNA microarray, and imaging means for picking up an image of an optical signal from the DNA microarray;

(3) fluid transporting section connected to the DNA microarray arranged on the stage of the microscope set forth in (2), to move a fluid into and out of the DNA microarray;

(4) a storage section which stores:

(a) programs indicating procedures and conditions for causing reaction in the DNA microarray in (1) while controlling all sections of the apparatus including the temperature regulating section in (2) and the liquid transporting section in (3) and then processing results obtained, and

(b) a score table indicating the type of the nucleic acid probe in (1) in association with coordinates of the nucleic acid probe in the DNA microarray;

(5) a main control section which controls the sections in (2) and (3) to operate the apparatus for the DNA microarray in (1) in accordance with a program stored in the storage section in (4), thus integrally controlling the whole apparatus;

(6) an image processing section which operates after the reaction based on the control by the main control section in (5), to process the image picked up by the imaging means set forth in (2) to determine the intensity of an optical signal for each of the probe spots, in accordance with a program contained in the storage section in (4); and

(7) an output section which searches the score table stored in the storage section in (4) to output, as determination results of gene examinations, data corresponding to the intensity of an optical signal from the coordinates determined by the image processing section in (6).

18. (Original) The apparatus utilizing a computer according to claim 17, wherein the DNA microarray comprises a porous film having a branching channel, and the nucleic acid probe is immobilized on an inner wall of the channel in the porous film.

19. (Original) A method of examining a gene using the apparatus according to claim 17, the method comprising;

(1) amplifying a nucleic acid extracted from a tissue or a cell obtained from a subject and adding an optical marker substance as a marker substance to afford a labeled nucleic acid;

(2) adding the labeled nucleic acid obtained in (1) to a DNA microarray comprising a desired nucleic acid probe;

(3) using the DNA microarray in (2) to cause hybridization reaction under desired conditions;

(4) measuring the intensity of an optical signal from the optical marker substance in the DNA microarray obtained in (3); and

(5) on the basis of the intensity of the optical signal obtained in (4), determining the amount of an expressed gene and/or whether or not any mutated gene is present, to obtain results of gene examinations.

20. (Original) A method of examining a gene using the apparatus according to claim 17, the method comprising;

(1) amplifying a nucleic acid extracted from a tissue or a cell obtained from a subject and adding an optical marker substance as a marker substance to afford a labeled nucleic acid;

(2) adding the labeled nucleic acid obtained in (1) to a DNA microarray comprising a desired nucleic acid probe;

(3) using the DNA microarray in (2) to cause hybridization reaction under desired conditions;

- (4) after the reaction in (3) has been finished, collecting a solution contained in the DNA microarray, at the bottom of the array;
- (5) measuring the intensity of an optical signal from the optical marker substance in the DNA microarray obtained in (3);
- (6) agitating again the liquid collected at the bottom of the array in (4);
- (7) using the DNA microarray in (6) to repeat hybridization reaction under desired conditions as required;
- (8) measuring the intensity of an optical signal from the DNA microarray obtained in (3); and
- (9) on the basis of the intensities of the optical signals obtained in (4) and (8), determining the amount of an expressed gene and/or whether or not any mutated gene is present, to obtain results of gene examinations.

21. (Original) The method according to claim 19, further comprising comparing information obtained by determining, on the basis of the intensity of the optical signal obtained in (4), the amount of an expressed gene and/or whether or not any mutated gene is present, with well-known information disclosed in a database and/or information obtained from a standard sample, thereby obtaining the results of gene examinations.

22. (Original) The method according to claim 20, wherein operations from (5) to (8) are repeated twice or more.